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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,185	08/03/2005	Gordon D. Ross	3593.1001-008	6460

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,185	ROSS ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 13-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4 sheets, 1/10/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 6/17/2008 has been received and entered into the present application.

Claims 1-14 are currently pending. Accordingly, claims 1-2 and 18 have been amended, claims 5-12 have been withdrawn and claim 15 has been cancelled.

As reflected by the attached, completed copy form PTO/SB/08A (three pages total), the Examiner has considered the cited reference.

Applicant's arguments, filed 6/17/2008 have been fully considered. Rejections not reiterated from the previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4; 13-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for the treatment of mammary carcinoma (specification page 8, Figure 5A-5D), the specification does not reasonably provide enablement for the treatment of <u>other</u> tumor types. The specification does not enable any person skilled in the art to which it pertains, or with which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988) as to undue experimentation. The factors include:

1) the nature of the invention

2) the breadth of the claims

3) the predictability or unpredictability of the art

4) the amount of direction or guidance presented

5) the presence or absence of working examples

6) the quantity of experimentation necessary

7) the state of the prior art

8) the relative skill of those skilled in the art

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The presently claimed invention is directed to a method of suppressing or eliminating tumor cells, by administering a therapeutically effective amount of neutral soluble glucan particles and an antitumor antibody.

In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the treatment of any tumor type could be effectively achieved by the administration of neutral soluble glucan and an antitumor antibody.

As set in In re Marzocchi et al., 169 USPQ 367 (CCPA 1971):

"[A] [s]pecification disclosure which contains the teachings of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support*, assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection

can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling." (emphasis added)

Here, the objective truth that any tumor type may be treated with a therapeutically effective amount of neutral soluble glucan and an antitumor antibody is doubted because, while the state of the art of cancer treatment is well developed with regard to the treatment of specific cancer types with specific chemotherapeutic agents regimes (see Cecil's Textbook of Medicine, pages 1060-1074), the state of the art with regard to treating all tumors using a single agent is grossly underdeveloped.

In this regard, Cecil's Textbook of Medicine (2000) is cited. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against treating all cancer types, nor is there any known anticancer agent or combination of agents that is effective against inhibiting the growth of any type of cancer cell. The Cecil reference clearly shows that for the various known cancer types, there is not one specific chemotherapeutic agent or combination thereof that is effective at treating cancer or inhibiting the growth of cancer cells for each and every type of cancer (see Table 198-5 at page 1065; Tables 198-6 and 198-7 at pages 1066; Table 198-8 at page 1068; and Table 198-9 at page 1071).

Given that there was not known any specific agent or combination of agents effective to treat al known types of cancer, one of ordinary skill in the art would not accept on its fact Applicant's statement that such an objective could be achieved in any type of tumor using the presently claimed neutral soluble glucan and an antitumor antibody without enabling a set of species representative of the full scope of cancers known in the art. The artisan would have required sufficient direction as to how, at minimum, a representative set of species of cancer could be effectively treated with neutral soluble glucan and an antitumor antibody, and, further, how the artisan could have reasonably extrapolated such results to the larger and highly varied genus of tumors in general without requiring undue experimentation to determine what types of tumors would actually show sensitivity to the presently claimed neutral soluble glucan and an antitumor antibody, such that the artisan would have been imbued with at least a reasonable

expectation of success in treating the tumor. Such success would not have been reasonably expected for all tumor types would not have been considered representative or suggestive of the same efficacy in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of structure and biochemical basis for the use of each agent, one of skill in the art would have no other recourse but undue experimentation to undertake extensive testing to determine which other tumor types would be amenable to treating using a therapeutically effective amount of neutral soluble glucan and an antitumor antibody.

It is in this regard that Applicant is directed to the MPEP 2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern in whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of enablement involved the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to use the *entire scope* of the claimed invention without undue experimentation.

A conclusion of lack of enablement must take into consideration the unpredictability in the art at the time of invention and the direction or guidance provided by Applicant. The amount of guidance required to present in the specification as originally filed is directed proportional to the amount of knowledge in the art as well as the unpredictability in the art. In other words, if little or nothing is known in the prior art about an aspect of the claimed invention and the art is unpredictable, the specification needs more detail and guidance as to how to use the invention in order to be enabling. Please reference In re Fisher, 417 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) and Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

The enablement of the working examples provided by the specification is not disputed. However, they are not representative of the breadth of the presently claimed subject matter. Applicant's claims broadly claim the use of a therapeutically effective amount of neutral soluble glucan and an antitumor antibody for *any tumor*. The fact that Applicant has exemplified use of this compound in mammary carcinoma cells does not address the high degree of variability in the art in terms of pathophysiological differences among tumor types and their reactivity to different anticancer compounds. Applicant has also failed to provide any evidence, or describe any protocol, that addresses this variability in the art such that one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success in treating any tumor with the claimed compound based on the direction provided in the present specification. While the lack of a working embodiment cannot be the sole factor in determining enablement, the absence of substantial evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the Wands factors as a whole.

In light of such, it is clear that one of ordinary skill in the art would be faced with the impremissible burden of undue experimentation in order to execute the entire scope of the subject matter presently claimed. The basis of the present rejection is not simply that experimentation would be required, since it is clear form the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction of Applicant would be *undue*. Please reference In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *if experimentation is necessary, it is undue*" (emphasis added). Given the high degree of unpredictability noted and recognized in the art with regard to the treatment of tumors, the state of art clearly precludes the general

exploitation of the results seen in two tumor types to the larger and much more highly varied genus of tumors as a whole. In the absence of any direction or guidance presented by Applicant as to how such a therapeutic objective could be achieved without necessitating an undue level of experimentation, the present disclosure is viewed as lacking an enabling disclosure of the *entire scope* of the presently claimed subject matter.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor with several years of experience in the art.

Applicant's Remarks

Applicant argues that the combination of whole glucan particles with an antitumor antibody is not a single agent and that the term "antitumor antibody" reflects a general category of antibodies, even though there is a specific antibody used for each type of tumor. Further, it is argued that whole glucan particles work synergistically with each antitumor antibody for the particular tumor targeted. Additionally, applicant argues that further experimentation necessary is not undue since the inventors have "determined a basic mechanism of action." Finally, Applicant alleges that the specification does not include all antibodies but a narrowed class.

Response to Applicant's Arguments

Applicant's amendments and remarks have been carefully considered in their entirety, but fail to be persuasive in establishing error in the propriety of the present rejection.

Examiner notes that the instant rejection is drawn to the treatment of other tumor types for which Applicant has not provided working examples of efficacy. With regards to Applicants claim that "antitumor antibody" reflects a general category of antibodies, Examiner reminds Applicant that a specie election has been made for one antitumor antibody, where Applicant elected trastuzumab. Additionally, Applicant alleges that the combination is synergistic and therefore this unexpected characteristic renders it as not anticipated by the reference, but advances no specific reason or evidence, aside from Counsels'

own speculation, in support of this position. This assertion by Counsel is an unsupported allegation and fails to take place of evidence in the record. Statements of this nature are clearly unpersuasive in accordance with guidance provided at MPEP 2145, which states, "The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602 145 USPQ 716, 178 (CCPA 1965); In re Geisler 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)." Accordingly, there is no reason or basis advanced by Applicant to reasonably assume or infer that a synergistic effect dose in fact occur, as a result, such an argument is unpersuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4; 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over James et al. (provided by Applicant) in view of Leyland-Jones (The Lancet, Oncology Vol.3, March 2002).

Jamas et al. discloses a neutral soluble beta glucan without stimulating the production of certain cytokines (abstract, lines 1-5). Furthermore, "unlike soluble glucans described by the prior art, the neutral soluble glucan of this invention neither induces nor primes IL-1 and TNF production in vitro or in vivo" (abstract, lines 11-13). Jamas et al. teaches that "the use of soluble and insoluble beta glucans alone or as vaccine adjuvants for viral and bacterial antigens has been shown in animal models to markedly increase resistance to a variety of bacterial, fungal..." (column 1, last 4 lines). The neutral soluble beta glucan has a "unique triple helical conformation" (column 4, lines 57-61). Finally, Jamas et al. discloses that "the neutral soluble glucan preparation is appropriate for parenteral... administration to humans and animals" (column 4, lines 1-4).

Leyland-Jones teaches that trastuzumab is the first clinically available oncogene-targeted therapeutic agent for treatment of solid tumors (see abstract). The author further states that the possibility of introducing this agent into the adjuvant setting and the introduction of new combinations, doses and schedules remaining exciting options (discussion, last paragraph). Additionally, the author discloses that trastuzumab provides a model of integration of new gene-targeted therapies (discussion, last paragraph).

One of ordinary skill in the art would have been motivated to combine the above teachings and as combined would teach the inventions as claimed. One of ordinary skill in the art would have been motivated by Jamas et al. and Leyland-Jones because both are directed to the treatment of tumors. The idea of combining the teachings of Jamas et al. and Leyland-Jones flows logically from having been individually taught by the prior art.

Applicant's Remarks

Applicant alleges that neither reference indicates that whole glucan particles act synergistically with antitumor antibodies to treat tumors as recited in Applicant's claims. Further, it is argued that at best the expectation would be that each component acts through separate mechanisms possibly to result in an additive effect.

Response to Applicant's Arguments

Applicant's amendments and remarks have been carefully considered in their entirety, but fail to be persuasive in establishing error in the propriety of the present rejection.

Applicant alleges that the combination is synergistic and therefore this unexpected characteristic renders it as not anticipated by the reference, but advances no specific reason or evidence, aside from Counsels' own speculation, in support of this position. This assertion by Counsel is an unsupported allegation and fails to take place of evidence in the record. Statements of this nature are clearly unpersuasive in accordance with guidance provided at MPEP 2145, which states, "The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602 145 USPQ 716, 178 (CCPA 1965); In re Geisler 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)." Accordingly, there is no reason or basis advanced by Applicant to reasonably assume or infer that a synergistic effect dose in fact occur, as a result, such an argument is unpersuasive in establishing nonobviousness of the claimed invention.

Conclusion

No claim remains to be found allowable.

a. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614